REMARKS/ARGUMENTS

Applicants note that the Examiner found the above-referenced Application eligible for continued examination under 37 C.F.R. § 1.114 and accordingly withdrew the finality of the Office Action dated November 19, 2003 and entered Applicants' submission filed February 19, 2004.

Claims 73-83 were pending in this Application.

Amendments to the Specification

The specification has been amended to correct minor clerical/typographical errors. No new matter has been added by way of these amendments.

Amendments to the Claims

Claims 73-77 and 79-83 have been amended. Claims 73 and 74 have been amended to specify that the claimed pharmaceutical preparation comprises a "protein" with specified structural and functional limitations, rather than a "FRIL family member molecule," and to indicate that the protein preserves "hematopoietic" progenitor cells. Support for these amendments can be found throughout the specification, where the proteins of the invention are described. Claim 75 has been amended to be in independent format. Claims 76-77 and 79-83 have been amended to recite additional claim dependencies. Claim 79 has also been amended to recite "pharmaceutical formulation" instead of "pharmaceutical carrier." Claims 81-83 have also been amended to recite "protein" instead of "FRIL family member molecule."

Claim 84 has been newly added. Claim 84 is directed to some of the subject matter of previous claim 75.

No new matter has been added by way of these amendments.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 73 and 75-80 were rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. The Office Action stated that the recitation of "hybridizing under stringent conditions" in claim 73 was ambiguous.

Applicants respectfully traverse this rejection.

The test for definiteness under 35 U.S.C. § 112, second paragraph, is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). Applicants respectfully assert that one skilled in the art would be readily able to ascertain the meaning of the phrase "hybridizes under stringent conditions" in light of Applicants' specification. The specification discloses what is meant by the above-mentioned phrase, for example, at page 21, line 19 to page 22, line 21. Furthermore, Applicants respectfully assert that at the time of the filing of this application, the above-mentioned phrase would have been readily understood by one of ordinary skill in the art, as it was, and still is, an established term in the art.

Indeed, recently issued U.S. patents include claims to nucleic acids which "hybridize under stringent conditions" to the complements of specifically disclosed sequences, without further limitations or description of that phrase. For example, the Examiner's attention is directed to U.S. Patent No. 6,756,491 (*e.g.*, claims 19, 25, 28 and 29), U.S. Patent No. 6,746,866 (*e.g.*, claim 2), U.S. Patent No. 6,734,293 (*e.g.*, claim 2), and U.S. Patent No. 6,733,965 (*e.g.*, claim 2), each of which issued in the last few months. The use of this phrase in the claims of issued U.S. patents, without further limitations or description, is evidence that the phrase is known in the art and is not vague or indefinite.

Accordingly, Applicants respectfully assert that the requirements of 35 U.S.C. § 112, second paragraph have been met with regard to the above-mentioned phrase and request withdrawal of this rejection.

Rejections Under 35 U.S.C.§ 112, First Paragraph

(a) Claims 73-80 were rejected under 35 U.S.C. § 112, first paragraph, for purportedly failing to provide an enabling disclosure.

Applicants respectfully traverse this rejection.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without

undue experimentation. *United States v. Telectronics Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirements of 35 U.S.C. § 112 is satisfied. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

In the instant application, four independent claims are pending (claim 73, 74, 75 and 84). Independent claim 73 is directed to a pharmaceutical formulation comprising (a) a pharmaceutically acceptable carrier; and (b) a protein that (1) binds to a normally glycosylated FLT3 receptor; (2) is encoded by a first nucleic acid molecule that hybridizes under stringent conditions to a second nucleic acid having a nucleotide sequence complementary to a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 5, and SEQ ID NO: 7; and (3) preserves hematopoietic progenitor cells.

Independent claim 74 is directed to a pharmaceutical formulation comprising (a) a pharmaceutically acceptable carrier; and (b) a protein that (1) binds to a normally glycosylated FLT3 receptor; (2) has at least 95% amino acid sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 6, and SEQ ID NO: 8; and (3) preserves hematopoietic progenitor cells.

Independent claim 75 is directed to a pharmaceutical formulation comprising (a) a pharmaceutically acceptable carrier; and (b) a protein that (1) binds to a normally glycosylated FLT3 receptor; (2) is encoded by a first nucleic acid molecule that hybridizes under stringent conditions to a second nucleic acid having a nucleotide sequence complementary to a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 5, and SEQ ID NO: 7; and (3) reduces a progenitor-cell depleting activity in a subject undergoing a therapeutic treatment having progenitor-cell depleting activity.

Independent claim 84 is directed to a pharmaceutical formulation comprising (a) a pharmaceutically acceptable carrier; and (b) a protein that (1) binds to a normally glycosylated FLT3 receptor; (2) has at least 95% amino acid sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 6, and SEQ ID NO: 8; and (3) reduces a progenitor-cell depleting activity in a subject undergoing a therapeutic treatment having progenitor-cell depleting activity.

Applicants note that the enablement rejection made in the Office Action focuses almost entirely on the structural limitations of independent claims 73 and 74: that the protein either (a) is encoded by a nucleic acid that hybridizes under stringent conditions to the complement of one of the three disclosed nucleotide sequences (claim 73), or (b) has at least 95% amino acid sequence identity to one of the three disclosed amino acid sequences (claim 74). However, all four currently pending independent claims include both structural and functional limitations. Thus, the pharmaceutical formulation of the invention comprises a protein that ***not only*** meets the structural limitations required of its nucleotide or amino acid sequence, ***but also*** meets the functional limitations of (a) binding to a normally glycosylated FLT3 receptor and (b) either preserving hematopoietic progenitor cells or reducing a progenitor cell depleting activity.

In this context, Applicants respectfully submit that the application as filed provides more than adequate guidance for one of ordinary skill in the art to make and use the claimed invention without undue experimentation. For example, the application teaches the methods used to isolate and purify three different FRIL proteins (*see, e.g.,* Example 1; Example 5; and Example 22); the nucleic acid and amino acid sequences of these three representative proteins (*see, e.g.,* pages 55-56; page 83 and pages 120-121); guidance for identifying new proteins (*see, e.g.,* page 50, line 8 through page 51, line 16); specific methods and assays to determine whether an isolated protein binds the FLT3 receptor (*see, e.g.,* Example 2), and specific methods and assays to determine whether an isolated protein preserves progenitor cells (*see, e.g.,* page 22, line 22 through page 23, line 10). Applicants respectfully submit that their disclosure of several representative members of the claimed genus of proteins, in addition to the description of common structural and functional characteristics shared by all family members, is more than sufficient to enable the ordinary artisan to practice the invention, as claimed, without undue experimentation. Following the guidance provided by the specification, the skilled artisan could easily identify or design a

protein based on its structural characteristics (*i.e.*, percentage amino acid sequence identity to one of the three disclosed amino acid sequences, or sufficient nucleotide sequence identity to hybridize under stringent conditions to one of the three disclosed nucleotide sequences) in combination with its functional characteristics (*i.e.*, ability to bind to a normally glycosylated FLT3 receptor and ability to preserve hematopoietic progenitor cells or reduce a progenitor cell depleting activity).

Applicants' claims 74 and 84 require at least 95% amino acid sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 6, and SEQ ID NO: 8. Applicants note, however, that the percentage identity between Dl-FRIL and Pv-FRIL is about 63%, while the percentage identity between Dl-FRIL and Yam-FRIL is about 65%. Clearly, therefore, Applicants have enabled the invention with respect to proteins with amino acid sequence identity that is significantly lower than the claimed 95%, and have demonstrated that three such proteins share the disclosed functional characteristics required for the claimed invention.

In summary, Applicants respectfully submit that, in light of the disclosure in the specification, as filed, and the level of skill in the art, no more than routine experimentation would be required to make and use the full scope of the claimed invention.

Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph (enablement), be reconsidered and withdrawn.

(b) Claims 73-80 were rejected under 35 U.S.C. § 112, first paragraph, for purportedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that, at the time the application was filed that the inventors had possession of the claimed invention.

Applicants respectfully traverse this rejection.

The Office Action relies on *Regents of the University of California v. Eli Lilly & Co.*, 119 F. 3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997) for the proposition that a description of a genus of FRIL family member sequences may be achieved by means of a recitation of a representative number of polypeptide sequences, defined by amino acid sequences falling within the scope of the genus, or of a recitation of structural features common to the genus, which

features constitute a substantial portion of the genus (*see,* Office Action, page 7, second full paragraph). The Office Action relies on *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, for the proposition that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

Applicants submit that the full scope of the pending claims is fully described in the specification as required by both *Eli Lilly* and *Vas-Cath*.

As described in detail in the response filed February 19, 2004, there is literal support in the specification, including the originally filed claims, for each and every claim limitation. This literal support includes experimental evidence demonstrating the identification, cloning, sequencing, site-specific mutagenesis, and functional characterization of representative members of the FRIL family of progenitor cell preservation factors. Therefore, the specification does, in fact, reasonably convey that the inventors were in possession of the presently claimed inventions at the time of filing.

At the time of the filing of the instant application, the general process of identifying nucleic acids by stringent hybridization and the general process of comparing polypeptides by amino acid sequence identity to a given sequence was routine. Moreover, as noted above, Applicants disclose three representative members of the claimed genus which fall well below the claimed level of identity (*e.g.*, about 63% identity between Dl-FRIL and Pv-FRIL, about 65% identity between Dl-FRIL and Yam-FRIL). Therefore, one of skill in the art would not only conclude that Applicants were in possession of the claimed genus but, in fact, were in possession of a broader genus.

Furthermore, the specification teaches methods and assays for assessing the claimed functional limitations of the claimed genus. Applicants disclose three proteins which meet these functional limitations despite the fact that they possess only about 63-65% amino acid sequence identity. Therefore, again, one of skill in the art would not only conclude that Applicants were in possession of the claimed genus but, in fact, were in possession of a broader genus.

Thus, Applicants disclose a representative number of species, describe both structural and function limitations that are met by these members, and provide guidance for the identification or design of additional members. Therefore, Applicants submit that the disclosure is adequate to

convey to the skilled artisan that Applicants were in possession of the claimed invention at the time of filing.

Accordingly, Applicants submit that the claimed invention is adequately described and respectfully request that the rejection under 35 U.S.C. § 112, first paragraph (written description), be reconsidered and withdrawn.

Objections

Claims 81-83 were objected to as being dependent upon a rejected base claim. Based on the foregoing remarks and arguments, Applicants respectfully request that this objection be withdrawn and reconsidered.

CONCLUSION

Claims 73-84 are pending in the Application. Applicants submit that the claims, as they currently stand, are in condition for allowance.

Applicants believe that no fees are required with the instant filing. However, in the event that any additional fees are required to maintain the pendency of this application, the Commissioner is hereby authorized to charge any such fees, or to credit any overpayments, to Attorney Deposit Account No. 08-0219.

Applicants respectfully request that the Examiner reconsider the application and claims in light of the foregoing amendments and remarks. If the Examiner believes that a telephone interview would be help expedite the successful prosecution of the claims, the undersigned attorney would be grateful for the opportunity to discuss any outstanding issues.

Respectfully submitted,

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